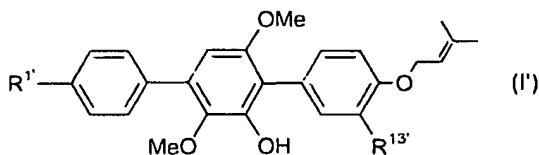


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CI  
cont  
other than hydrogen, and excluding a product compound of the  
formula (I'):



wherein  $R^{1'}$ , is hydrogen or hydroxy and  $R^{13'}$  is hydroxy or methoxy,  
pharmaceutically acceptable salt, hydrate or prodrug thereof.--

#### REMARKS

Claims 28-54 are pending in the present application. Support for claims 28-54 can be found in claims 1-27, respectively, with the exception that claims 53-54 recite the definitions of cancelled claims 18-19. No new matter has been added by way of the above-amendment.

The Examiner has required election in the present application between:

Group I, claims 34-41, 45-49 and 52 (originally claims 7-14, 18-22 and 25), drawn to a compound of formula (I) and composition;

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Group II, claims 42-44, and 43-54 (originally 15-17 and 16-27), drawn to processes for making a compound of formula (I); and

Group III, claims 28-33 and 50-51 (originally claims 1-6 and 23-24), drawn to an immunosuppressor of IgE.

For the purpose of examination of the present application, Applicants elect, with traverse, Group I, claims 34-41, 45-49 and 52 (originally claims 7-14, 18-22 and 25).

Applicants respectfully request that Group I be rejoined with Group II, since both Groups I and II have a single general inventive concept.

Based upon the decision in Caterpillar Tractor Co. v. Commissioner of Patents and Trademarks, 231 USPQ 590 (E.D. Va. 1986), the Patent and Trademark Office now must consider applications filed under 35 USC 371, by following PCT Rule 13.1 and 13.2 when considering unity of invention of claims of different categories without regard to the practice in national applications filed under 35 USC 111.

The MPEP instructs (at page 1800-47, column 2, revised Feb. 2000), that the

method for determining unity of invention under PCT Rule 13 shall be construed as permitting, in particular, the

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inclusion of any one of the following combinations of claims of different categories in the same international application:

(A) In addition to an independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product, and an independent claim for a use of the said product...

Thus, it is proper to keep the processes of forming the inventive compounds of formula (I) with the compounds of formula (I), since the special technical feature (compounds of formula (I)) are common to both Groups I and II.

In the event that the Examiner rejoins Groups I and II, Applicants also elect, with traverse, the specific process of claim 15 for examination on the merits.

On page 3 of the outstanding Office Action, the Examiner requests clarification as to whether claims 18-21 are the same as claims 7-12 and the process claims 25-27 are the same as process claims 15-17.

There are fewer groups recited for variable "Y" in claims 18-19 than in claim 7. Also, there are fewer groups recited for variables "Y" and "-X-Y" in claims 20-21 than in claim 19.

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Claims 26 and 27 recite a process for preparing the compounds of claims 18-22, and as such are different than process claims 16-17.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Garth M. Dahlen, Ph.D. (Reg. No. 43,575) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH &amp; BIRCH, LLP

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By [Signature] #43575  
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MSW/GMD/bsh  
0032-0248P

Enclosed: 1) Article 34 Amendment

(Rev. 01/22/01)

## AMENDMENT

To: Commissioner of the Patent Office

(To: KARAKI, Ichiyo, Examiner of the Patent Office)

1. Identification of the International Application

PCT/JP97/02635

2. Applicant (Common Representative)

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Osaka 541-0045 JAPAN

4. Date of Invitation 10.02.98

5. Item to be Amended

CLAIMS

6. Subject Matter of Amendment

As per the attached sheets

Claims 18 to 25 are added.

Claims wherein the substituents are restricted are added as Claims 18 to 21.

A claim wherein "or" in Claim 7 (l. 8 and l. 12, p. 475) is amended to "and" and the compounds described in the cited reference 3 to 6 are excluded is added as Claim 22.

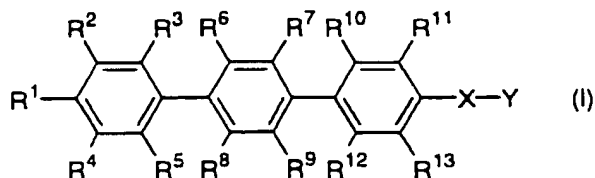
A claim which claims a pharmaceutical composition comprising the compounds claimed in Claims 18 to 22 is added as Claim 23.

Claims which claim a process for producing the compound claimed  
in Claims 18 to 22 are added as Claims 24 and 25.

7. List of Attached Documents

New pages of CLAIMS 484/1, 484/2, 484/3, 484/4, 484/5 and 484/6

18.(New) A compound of the formula (I):



wherein  $R^1$  is hydrogen, halogen, optionally substituted lower alkenyloxy, optionally substituted lower alkylsulfonyloxy, optionally substituted amino or optionally substituted sulfamoyl,

$R^2$  is hydrogen, halogen or lower alkyl having 1 to 3 carbon atoms,

$R^3$  is hydrogen or halogen,

$R^4$  is hydrogen, lower alkyl, lower alkoxy or halogen,

$R^5$  is hydrogen, lower alkoxycarbonyl or carboxy,

$R^6$  is hydrogen, lower alkyl or halogen,

$R^7$  is hydrogen, lower alkyl or lower alkoxy,

$R^8$  is hydrogen, lower alkyl or lower alkoxy,

$R^9$  is hydrogen, hydroxy, carboxy, optionally substituted lower alkyl, optionally substituted lower alkoxy, optionally substituted lower alkenyl, optionally substituted lower alkoxycarbonyl, optionally substituted lower alkylsulfonyloxy, formyl, optionally substituted carbamoyl or optionally substituted amino,

$R^{10}$  is hydrogen,

$R^{11}$  is hydrogen or halogen,

$R^{12}$  is hydrogen,

$R^{13}$  is hydrogen, hydroxy, halogen, carboxy, optionally substituted lower alkyl, optionally substituted lower alkoxy, optionally substituted acyloxy, optionally substituted lower alkylsulfonyloxy, formyl or optionally substituted amino,

X is  $-O-$ ,  $-NH-$ ,  $-NMe-$  or  $-SO_2-$ ,

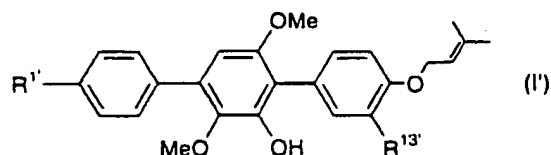
Y is lower alkyl optionally substituted with lower alkoxycarbonyl, aryl, lower alkylaryl, halogenoaryl, lower alkoxyaryl, heterocyclyl or acyl; or lower alkenyl optionally substituted with hydroxy, halogen or aryl,

and  $R^1$  and  $R^4$  or  $R^8$  and  $R^9$  taken together may form a 5- or 6-membered ring which contains one or more of O,

excluding compounds wherein one or more of  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are halogen and the others are hydrogen and compounds wherein all of  $R^2$ - $R^{13}$  are hydrogen, provided that  $R^1$  is not hydrogen or fluorine, all of  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^{12}$  are hydrogen, or  $R^{13}$  is not hydrogen or halogen when  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are all simultaneously hydrogen,

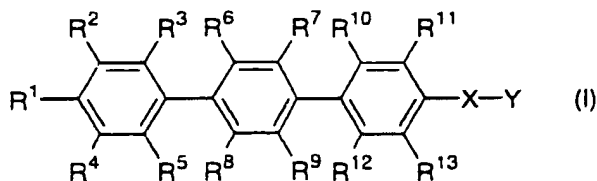
and further provided that  $R^{13}$  is not hydrogen or -X-Y is not methoxy when at least one of  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  is a substituent other than hydrogen,

and excluding a compound of the formula (I'):



wherein  $R^{1'}$  is hydrogen or hydroxy and  $R^{13'}$  is hydroxy, pharmaceutically acceptable salt, hydrate or prodrug thereof.

19.(New) A compound of the formula (I):



wherein  $R^1$  is hydrogen, hydroxy, halogen, optionally substituted lower alkoxy, optionally substituted alkenyloxy, optionally substituted lower alkylsulfonyloxy, optionally substituted amino or optionally substituted sulfamoyl,

$R^2$  is hydrogen, halogen or lower alkyl having 1 to 3 carbon atoms,

$R^3$  is hydrogen or halogen,

$R^4$  is hydrogen, lower alkyl, lower alkoxy or halogen,

$R^5$  is hydrogen, lower alkoxy carbonyl or carboxy,

$R^6$  is hydrogen, lower alkyl or halogen,

$R^7$  is hydrogen, lower alkyl or lower alkoxy,



R<sup>8</sup> is hydrogen, lower alkyl or lower alkoxy,

R<sup>9</sup> is hydrogen, hydroxy, carboxy, optionally substituted lower alkyl, optionally substituted lower alkoxy, optionally substituted lower alkenyl, optionally substituted lower alkoxycarbonyl, optionally substituted lower alkylsulfonyloxy, formyl, optionally substituted carbamoyl or optionally substituted amino,

R<sup>10</sup> is hydrogen,

R<sup>11</sup> is hydrogen or halogen,

R<sup>12</sup> is hydrogen,

R<sup>13</sup> is hydrogen, hydroxy, halogen, carboxy, optionally substituted lower alkyl, optionally substituted lower alkoxy, optionally substituted acyloxy, optionally substituted lower alkylsulfonyloxy, formyl or optionally substituted amino,

X is -O-, -NH-, -NMe- or -SO<sub>2</sub>-,

Y is lower alkyl optionally substituted with aryl; or lower alkenyl,

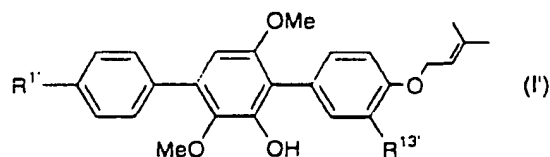
and R<sup>1</sup> and R<sup>4</sup> or R<sup>8</sup> and R<sup>9</sup> taken together may form a 5- or 6-membered ring which contains one or more of O,

excluding compounds wherein one or more of R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are halogen and the others are hydrogen and compounds wherein all of R<sup>2</sup>-R<sup>13</sup> are hydrogen,

provided that R<sup>1</sup> is not hydrogen, fluorine or optionally substituted lower alkoxy, all of R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>12</sup> are hydrogen, or R<sup>13</sup> is not hydrogen or halogen when R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are all simultaneously hydrogen,

and further provided that R<sup>13</sup> is not hydrogen or -X-Y is not methoxy when at least one of R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> is a substituent other than hydrogen,

and excluding a compound of the formula (I'):



wherein R<sup>1'</sup> is hydrogen or hydroxy and R<sup>13'</sup> is hydroxy,

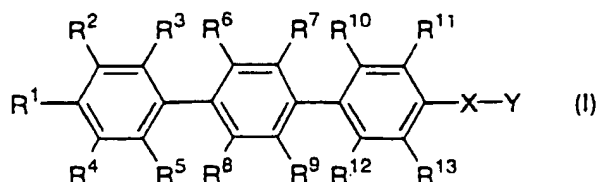
pharmaceutically acceptable salt, hydrate or prodrug thereof.

20.(New) The compound, pharmaceutically acceptable salt or hydrate thereof

claimed in claim 19 wherein Y is methylbutenyl.

21.(New) The compound, pharmaceutically acceptable salt or hydrate thereof claimed in claim 19 wherein -X-Y is  $-\text{OCH}_2\text{CH}=\text{CMe}_2$  or  $-\text{OCH}_2\text{C}_6\text{H}_5$ .

22.(New) A compound of the formula (I):

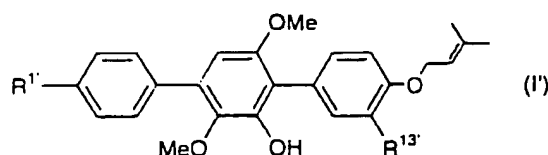


wherein  $\text{R}^1, \text{R}^2, \text{R}^3, \text{R}^4, \text{R}^5, \text{R}^6, \text{R}^7, \text{R}^8, \text{R}^9, \text{R}^{10}, \text{R}^{11}, \text{R}^{12}$  and  $\text{R}^{13}$  are each independently hydrogen, hydroxy, halogen, carboxy, optionally substituted lower alkyl, optionally substituted lower alkoxy, optionally substituted lower alkenyl, optionally substituted lower alkenyloxy, optionally substituted lower alkylthio, optionally substituted lower alkoxycarbonyl, optionally substituted acyloxy, optionally substituted lower alkylsulfonyl, optionally substituted lower alkylsulfonyloxy, optionally substituted lower alkylsulfinyl, nitro, cyano, formyl, optionally substituted amino, optionally substituted carbamoyl, optionally substituted sulfamoyl or optionally substituted heterocyclyl,

X is  $-\text{O}-, -\text{CH}_2-, -\text{NR}^{14}-$  wherein  $\text{R}^{14}$  is hydrogen, optionally substituted lower alkyl, optionally substituted lower alkenyl or acetyl, or  $-\text{S}(\text{O})_p-$  wherein p is an integer of 0 to 2,

Y is optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, optionally substituted acyl, optionally substituted cycloalkyl, optionally substituted cycloalkenyl, optionally substituted aryl or optionally substituted heterocyclyl, and Y may be optionally substituted lower alkoxy when X is  $-\text{CH}_2-$  and may be optionally substituted lower alkoxycarbonyl, optionally substituted lower alkylsulfonyl or optionally substituted arylsulfonyl when X is  $-\text{O}-$  or  $-\text{NR}^{14}-$ ,  $\text{R}^1$  and  $\text{R}^4, \text{R}^1$  and  $\text{R}^2, \text{R}^2$  and  $\text{R}^3, \text{R}^4$  and  $\text{R}^5, \text{R}^6$  and  $\text{R}^7, \text{R}^8$  and  $\text{R}^9, \text{R}^{10}$  and  $\text{R}^{11}, \text{R}^{12}$  and  $\text{R}^{13}, \text{R}^{11}$  and  $-\text{X}-\text{Y}$ , or  $\text{R}^{13}$  and  $-\text{X}-\text{Y}$  taken together may form a 5- or 6-membered ring which may contain one or more of O, S or  $\text{NR}^{15}$  wherein  $\text{R}^{15}$  is

hydrogen, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted arylsulfonyl and which may optionally be substituted, excluding compounds wherein one or more of  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are halogen and the others are hydrogen, compounds wherein all of  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are halogen and compounds wherein all of  $R^2$ - $R^{13}$  are hydrogen, halogen or cyano, provided that  $R^1$  is not hydrogen, fluorine, optionally substituted lower alkyl or optionally substituted lower alkoxy, all of  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$  and  $R^{12}$  are hydrogen, and  $R^{13}$  is not hydrogen or halogen when  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are all simultaneously hydrogen, and further provided that  $R^1$  is not methyl or acetyloxy,  $R^{13}$  is not hydrogen, optionally substituted lower alkoxy, optionally substituted carbamoyl, and  $X-Y$  is not methoxy when at least one of  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  is a substituent other than hydrogen, and excluding a compound of the formula (I'):



wherein  $R^{1'}$  is hydrogen or hydroxy and  $R^{13'}$  is hydroxy or methoxy, pharmaceutically acceptable salt, hydrate or prodrug thereof.

23.(New) A pharmaceutical composition comprising the compound, pharmaceutically acceptable salt, hydrate or prodrug thereof claimed in any one of claims 18-22.

24.(New) A process for producing a compound of the formula (I), pharmaceutically acceptable salt or hydrate thereof according to any one of claims 18-22 comprising reacting a compound of the formula (IV') with a compound of the formula (V), followed by reacting a compound of the formula (VI) according to claim 16.

25.(New) A process for producing a compound of the formula (I), pharmaceutically acceptable salt or hydrate thereof according to any one of claims 18-22 comprising reacting a compound of the formula (IV'') according to claim 17 with a compound of the

formula (VI) according to claim 16, followed by reacting a compound of the formula (V) according to claim 16.